

work with the spectrophotometer did not substantiate this idea, however, as the ratios obtained for the light absorption at two given wave lengths ($\lambda = 5400$ and $\lambda = 5600$) are entirely different from those obtained in solutions of known methemoglobin content. Further work is necessary before any statement can be made as to the nature of this reduced oxygen carrying power. Such work is now in progress.

As a control a laparotomy without the removal of the spleen was performed on one rabbit. There was no discrepancy found between total and oxygen bearing pigments.

Two rabbits were not bled, except for the initial samples, until the fifth day after splenectomy. At that time both showed a definite loss in oxygen carrying hemoglobin, one of 6, the other of 12 per cent of the total pigment. Both had returned to normal relations by the twelfth day. This suggests the possibility that the stimulus of the daily bleedings, 5 to 7 cc. being taken at a time, may play some part in causing the more rapid return to normal in those rabbits that were bled frequently immediately after operation. Further experimentation is being carried on to clarify this point.

This is a preliminary report.

¹ Van Slyke, D. D., *J. Biol. Chem.*, 1926, lxxvi, 409.

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Gold Preparations in Therapy.

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Gold preparations have recently found clinical application in tuberculosis and certain diseases of the skin. Among these preparations are Sanocrysin or gold and sodium thiosulfate, Krysolgan and Triphal.

Sanocrysin or gold and sodium thiosulfate was originally prepared by Fordos and Gellis in 1845. It has been improved on by Mollgaard and contains about 37.5 per cent gold and 26.2 per cent sulphur, which would correspond to the formula $3\text{Na}_2\text{S}_2\text{O}_3\text{Au}_2\text{S}_2\text{O}_3 \cdot 4\text{H}_2\text{O}$.

Triphal, one of the other preparations studied by us from a toxicological point of view, contains approximately 44 per cent gold and 7.1 per cent sulphur, and this corresponds to the chemical for-

mula $C_6H_3N-NH-CSAu-COONa \cdot 2H_2O$ or the sodium salt of Aurothiobenzimidazolcarboxylic acid.

Previous investigations¹ have shown that under some conditions, gold salts tend to produce marked kidney and liver damage as well as urticaria, pruritus and erythematous eruptions. With these possibilities in mind, the present report deals with a toxicological study of the three common gold preparations which are available.

Examination of Tables I, II and III, shows the effects of the injection of these drugs in normal Albino rats, with the action upon the lungs, liver and kidneys. The injections were carried out on normal healthy Albino rats from a common source; they were maintained on a constant, well balanced diet composed of whole wheat flour, corn meal, skim milk, calcium carbonate, and sodium chloride, together with the addition of 2 per cent of active cod liver oil.

Examination of these tables further shows definitely the marked difference in toxicity of these various preparations, and this observation alone has a distinct bearing on the clinical application of these drugs.

The clinical discussion will be found in another article.

TABLE I.
Toxicity of Krysolgan.*
Albino rats injected intravenously.

Dose mg./kg.	Rat No.	Length of life	Ending	Lungs	Liver	Kidneys	Remarks
1	1637	7 days	Killed	Normal	Normal	Normal	
1	1638	7 days	"	"	"	"	
2	1639	7 days	"	"	"	Enlarged nephrosis	Lost weight after injection
2	1640	7 days	"	"	"	"	"
3	1641	2 days	Died	Congest- ed pleur- al fluid increased	"	Nephrosis	Hemorrhages in thymus and ad- renals. Colon empty.
3	1642	3 days	"	"	Swollen and dark	"	Retroperitoneal tissue oedema- tous. Bladder empty and con- tracted.
4	1643	3 days	"	"	" "	"	
4	1644	3 days	"	"	" "	"	
5	1645	3 days	"	"	" "	"	
5	1646	3 days	"	"	" "	"	Retroperitoneal tissue oedema- tous.

* Krysolgan (according to Schering circular) is employed in doses of 0.0015 grain to 1.5 grains. In preparing the solution for the above Krysolgan toxicity test the contents of two 0.050 grain ampules (6.5 milligrams) were dissolved in 10 cc. freshly distilled water.

TABLE II.
Toxicity of gold and sodium thiosulphate.
Albino rats injected intravenously.

Dose mg./kg.	Rat No.	Length of life	Ending	Lungs	Liver	Kidneys	Remarks
40	1648	7 days	Killed	Normal	Normal	Normal	
40	1649	7 days	"	"	"	"	
60	1650	7 days	"	"	"	Enlarged nephrosis	Lost weight after injection
60	1651	7 days	"	"	"	" "	" "
80	1652	3 days	Died	"	"	" "	" "
80	1653	4 days	"	"	"	" "	" "
100	1654	2 days	"	"	Swollen and dark	" "	Small intestines congested. Colon empty.
100	1655	5 days	"	"	Normal	" "	
120	1656	4 days	"	"	"	" "	
120	1657	4 days	"	"	"	" "	

TABLE III.
Toxicity of Triphal.
Albino rats injected intravenously.

Dose mg./kg.	Rat No.	Length of life	Ending	Lungs	Liver	Kidneys	Remarks
80	1599	7 days	Killed	Normal	Normal	Normal	Gained in wgt. after injection.
80	1602	7 days	"	"	"	"	" "
80	1605	7 days	"	"	"	"	" "
100	1600	7 days	"	"	"	"	" "
100	1603	7 days	"	"	"	"	" "
100	1606	7 days	"	"	"	"	" "
120	1601	7 days	"	"	"	"	" "
120	1604	7 days	"	"	"	Swollen nephrosis	" "
120	1607	7 days	"	"	"	"	" "
140	1608	3 days	Died	"	"	Slight nephrosis	Colon empty.
140	1609	3 days	"	"	"	"	Colon contained well formed feces.

It might be stated at this time that the use of Triphal clinically, shows a cure in 77.2 per cent of the cases treated with Triphal as compared with about 30 per cent cures with the use of gold and sodium thiosulfate. These toxicity studies reported in Tables I, II and III, also indicate the importance of the removal of focal infections before the injection of gold salts of this nature. It will be readily seen from the toxicity table on Triphal that this drug, from a toxicological point of view, will serve as a safe effective means of application to the treatment of *Lupus erythematosus*.

These studies were carried out entirely with the idea of application to the treatment of skin diseases such as *Lupus erythematosus*, *Lupus vulgaris* and the tuberculids.

Of the three preparations examined, Triphal shows a much lower toxicity, greater stability in powder form and also in solution. Solutions of gold and sodium thiosulfate decompose readily, yielding a white precipitate and giving a marked odor of hydrogen sulfide.

This is a preliminary report.

¹ Bruck, C., and Glück, *Muchen, med. Wchnschr.*, 1913, ix, 57. Bruhns, C., *Dermat. Wochenschrift*, 1924, lxxix, 945. Galewsky, E., *Dermat. Wochenschr.*, 1924; *Arch. f. Derm. u. Syph.*, 1926, cli, 370. Jeanselme, E., and Burnier, R., *Bull. de la Soc. Franc. et de Syph.*, 1926, ix, 703. Martenstein, H., *Klin. Wochenschr.*, 1922, i, 2235; *Derm. Zeitschr.*, 1926, June, 309. Mollgaard, H., *Copenhagen, Nyt. Nordisk Forlag. Anold Busck*, 1924. Schamberg, J. F., and Wright, Carroll S., *Arch. Derm. Syph.*, 1927, xv, 119. Ullmann, K., *Wien. klin. Wochenschr.*, 1924, xxiii, 579.

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Carbon Dioxide and Bacterial Toxin Production: Preliminary Report on Diphtheria Toxin.

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Considerable difficulty is still being experienced in obtaining uniformly potent toxins, even under the best of known conditions. The purpose of this investigation has been to determine whether carbon dioxide bears any definite relationship to toxin production.

The commonly used medium containing meat infusion, 2 per cent Difco Proteose Peptone and 0.5 per cent NaCl was employed. The reaction was adjusted to pH 7.5. After clarification by heat, the filtered medium was distributed in 500 cc. Erlenmeyer flasks, 90 cc. to each flask. Final sterilization was accomplished by autoclaving at fifteen pounds pressure for fifteen minutes.

Immediately after cooling each flask was inoculated with 1 cc. of a 24 hour broth culture of *C. diphtheriae* (Park No. 8).

The inoculated flasks were divided into 4 sets, 4 flasks in each set, and incubated under the following conditions: 1 was incubated under ordinary conditions. 2 was aerated with air. 3 was aerated with carbon dioxide free air. 4 was aerated with an atmosphere containing 3 per cent carbon dioxide.

All aerated flasks were aerated at the rate of 100 cc. per hour, and incubation was at 37° C.

One flask was removed from each set at intervals of three, five, eight and 20 days from the time of inoculation, and the following